REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 1, 3, 4, 6, 8-11, 16 and 19 are in the case.

I. THE INTERVIEWS

At the outset, the undersigned wishes to thank the Examiner (Mr. Kosack) for kindly discussing the present application with the undersigned. The interviews were held on September 28, 2007 and October 16, 2007. The reason for the interviews was to discuss the outstanding obviousness rejection and proposed claim amendments. The substance of the interviews will be clear from the comments presented below.

II. THE 35 U.S.C. §112, SECOND PARAGRAPH, REJECTION

Claims 12-18 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for the reasons detailed on page 2 of the Action. In response, and without conceding to the merit of the rejection, claims 12-15 and 17-18 have been cancelled without prejudice. Claim 16 has been amended to specify that the nitroreductase enzyme is endogenous. Support for this amendment appears at page 40, line 20 of the specification. With this amendment, the claimed method does not require delivery of a gene to the cells because the enzyme is expressed naturally. It is therefore no longer necessary to specify steps for delivery of a gene and the promoters used. Claim 16 has also been amended to include the phrase "to activate the compound of formula (IIb) into an active metabolite to ablate the tumor cells", to clarify the mechanism of action of the compounds of formula (IIb). Support for this

amendment may be found on page 11, lines 5-10 of the specification. No new matter is entered.

Claims 20 and 21 have been rejected as providing for the use of compounds of Formula I. In response, claims 20 and 21 have been cancelled without prejudice.

Withdrawal of the outstanding 35 U.S.C. §112, second paragraph, rejection is now believed to be in order. Such action is respectfully requested.

III. THE 35 U.S.C. §101 REJECTION

Claims 20-21 stand rejected under 35 U.S.C. §101. In response, as noted above, these claims have been cancelled without prejudice.

IV. THE OBVIOUSNESS REJECTION

Claims 1-21 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Friedlos et al., *J. Med. Chem.* 1997, 1270-1275 in view of Patani et al., *Chem. Rev.* 1996, 3147-3176. That rejection is respectfully traversed.

As now claimed, the invention is directed to a nitroaniline-based unsymmetrical mustard represented by the Formula (IIb)as set forth in amended claim 1. For the reasons discussed below, it is believed that the invention as now claimed is clearly patentably distinguished over the art of record.

Without conceding to the merit of the assertions in the Action, and in order to expedite prosecution, the claims have been amended so as to be directed to the compounds of Formula IIb, that is compounds of formula I in which X and Y are meta and A and B (corresponding to X and Y of Friedlos) are different to each other. As

discussed during the interview, and as urged hereinbelow, it is believed that the invention as now claimed is not rendered unpatentable by Friedlos and Patani, alone or in combination. Subject matter canceled by the present amendment has been deleted without prejudice to pursuing that subject matter in a separate continuing application.

The compound in Friedlos that is the closest in structure to the compounds of formula IIb is compound 6. Compound 6 is an asymmetrical mustard compound. The claimed compounds of Formula IIb are not rendered unpatentable by compound 6 and/or the disclosures of Friedlos and Patani, taken alone or in combination. The compounds of Formula IIb have significant structural differences to compound 6. Thus, X and Y of the compounds of Formula IIb are meta to each other whereas in Friedlos the corresponding groups are para to each other. Moreover, Friedlos and Patani provide no motivation to one of ordinary skill, either alone or in combination, to make compounds which are so structurally distinct. Simply substituting the chloro group of compound 6 of Friedlos with another halogen, which the Action suggests is obvious in view of Patani for compounds of Formula IIa, would not yield a compound of Formula IIb.

Furthermore, all of the compounds in Friedlos with potency sufficient to suggest anti-cancer activity (compounds 8, 9, 13 and 14) require A and B to be the **same**. Compound 6, the only compound in which A and B are different, is referred to as "insufficiently potent to allow a full data set to be collected" (page 1272). Therefore, there is nothing in Friedlos which would have motivated the person of ordinary skill to synthesize compounds in which A and B are different with any expectation of those compounds having sufficient potency to be anti-cancer agents. Indeed, it is believed

that one of ordinary skill would have interpreted Friedlos as actually leading away from asymmetric mustard compounds and towards symmetric mustard compounds, which are the opposite of the compounds of Formula IIb.

For all of the above reasons, it is believed that the invention as now claimed is clearly patentably distinguished from Friedlos and Patani. Withdrawal of the obviousness rejection is respectfully requested.

V. OTHER CLAIM AMENDMENTS

Applicants wish to correct an obvious clerical error in claim 1 to insert an H which is missing from two of the definitions for Y. This means that the R_2 group in both cases should more correctly be expressed as an "alkylene" group (divalent) rather than an alkyl group. In view of this, the definition of R_2 has been amended to correct this obvious error by including lower alkylene. No new matter is entered.

Favorable action is awaited.

Respectfully submitted,

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